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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,006	04/12/2004	Andrea G. Cochran	11669.118USD1	5028

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EXAMINER

WESSENDORF, TERESA D

ART UNIT PAPER NUMBER

1639

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/823,006	Applicant(s) COCHRAN ET AL.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-27 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 19-27 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Status of Claims

Claims 19-27 are pending in the application and under examination.

Specification

The disclosure is objected to because of the following informalities: there are no Seq. ID. No. for the sequences recited at page 4, line 5, line 8 and line 17; page 26, line 9 and page 28, line 19.

Appropriate correction is required.

Applicants are requested to check for other Sequences in the specification to ensure that they have a corresponding Seq. ID. Nos.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicants' cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and

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use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the genus of the invention. Applicants at the time of the invention do not appear to be in possession of the claimed genus. The claimed genus recites for a method of constructing a library of structurally-constrained peptides. However, it contains only a single step i.e., synthesizing the library of peptides with a beta turn scaffold. It is not apparent from the claims how the synthesis is accomplished by the single process step. Neither is it apparent what is being synthesized in the absence of any primary sequence for the claimed library of peptide. As a skilled in the art appreciates, synthesis of peptides can only be accomplished if one has the

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primary sequence of the peptide, which then forms a secondary structure. The claims are more directed to describing the property of the peptides presented in beta structure, which recites the only two residue, Trp-Trp in the entire peptide sequence, not to a method step. It is does not describe the kind of synthesis for the numerous variables of the genus claims. For example, it does not describe the kind and length of the random amino acids consist in the beta turn that can be synthesized. The position of the Trp-Trp cross strand that forms a zipper-like motif without any disulfide bond, the number of said Trp-Trp in the scaffold. The type of constrained imposed on the beta turn structure scaffold. The claims contain too many variables for which not a single variable has been defined for any type of synthesis. Without a method steps for the genus claim with no primary structure, it is not seen how a library can be synthesized given the huge scope of any beta turn presented sequences. The huge scope of the genus claim cannot be adequately described only by a single species described in the specification. The specification describes the synthesis of a single species of the library having defined structure wherein Thr is varied to create a library. The disclosure further describes that the additional residues in the hydrogen bonding positions of the strands were taken from sequences used in the

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WO 00/77194. Reliance on this foreign Patent is improper as it not clear which of the other sequences are taken from this World Patent. Thus, the essential features of the claims described in the World Patent are missing in the instant description. Even for the specific sequences of trpzip4 in the WTW motif applicants disclose the need for compatibility of the specific variations with the trpzip scaffold. It is well known in the art that the features necessary for structural stability of natural peptides remain poorly understood. This is true in spite of extensive studies of the rules governing conformational preferences in natural peptides and the existence of several peptide library systems. To date there has been little systematic or quantitative assessment of the effect of residue substitutions and non-covalent interactions on structure. The specification, except for the specific variations of Thr in the WTW motif, does not provide a method by which the claimed library containing only two trp in a beta turn structure has been synthesized. It does not describe any other random residues that would be considered compatible to the beta turn structure. In biotechnological invention one cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. Applicants, at the time of

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filing, are deemed to have not invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). More importantly, there is no description in the specification as to the use of the obtained library. The specification, specifically the Examples, describe a study of the effects of the different variations in the Thr residues. It does not describe completely the use of said study in terms of the utility requirement of patent law.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

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Claim 19 is confusing as to the library of peptide being synthesized. Is the library of peptides contained in the presented turn sequence itself the library or a part thereof? If only a part which part of this turn sequence is randomized and which is not? Is a library different from the recited plurality of peptides? The phrase "zipper-Like motif " renders the claim(s) indefinite because the claim(s) include(s) elements or residues not actually disclosed thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cochran et al (WO 0077194).

Cochran discloses at page 15, line 13 up to page 23, line 6 a method of synthesizing a library of peptide containing a W-W cross strand. Cochran states that many methods for generating

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peptide libraries that are known in the art can be used to generate the libraries of the instant invention. Cochran further discloses at page 9, line 23 up to page 10, line 27 that disulfide cyclization is helpful, although not sufficient to constrain the structure of many peptides. The rest of the residues of the peptide are further selected to be significantly biased toward the formation of the hairpin structure. A subset of the residues within the peptide of the invention is varied to provide relative diversity for mimicking various bioactive peptides having a identified secondary structure, such as beta turn. Cochran further states at page 10, lines 22-29 that "... variations can occur at non-hydrogen bonded strand sites (e.g., A1/A5).... and its cross -strand counterpart(e.g., A1/A5 or A2/A4) can have same or different amino acids..." See also page 14, lines 6-10 wherein Cochran made an analogy to the WW domains. Cochran discloses or at least suggests that D-cys at one or both ends was not compatible with the cross-strand geometry of hairpins (as initially thought of said disulfide bond geometry). Since Cochran discloses or at least suggests the WW domains hence, it would be within the ordinary skill in the art to pick and choose the specific residues taught in the generic formula. The suggested teachings of Cochran that cys has not been used before would have led one to remove the cys

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residues especially since Cochran discloses that the cross strand occurs between the W-W residues. Note that Cochran discloses or directs primarily the experiments to the peptide sequence responsible for the turn sequence (without the presence of Cys).

Claims 19-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson et al (US 6,878,804) in view of Floudas et al (US 2003/0036093).

Robinson et al discloses at col. 5, line 47 up to col. 7, line 10 a method of constructing a library of structurally-constrained peptides comprising the synthesis of template-fixed cyclic peptides of general formula I which mimic the various naturally occurring beta-hairpin conformations (see e.g. the Figures, Example 1). Template structures corresponding to above formulae (a) through (h) have been shown to stabilize the H-bond network present in beta-hairpins. The beta-hairpin motif consists of two antiparallel beta-strands linked by a short loop or turn and have been classified depending on the H-bonding network. Robinson discloses that in large surface protein interfaces, there are hot spots of binding energy made up of a small subset of residues in the dimer interface. These hot spots are enriched in tryptophan (Trp), tyrosine (Tyr) and arginine (Arg), and are surrounded by energetically less important

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residues. The beta-hairpin loop motif offering two opposite beta-sheet surfaces (e.g. a hydrophobic and a hydrophilic face) for possible binding interactions is ideally suited to meet the criteria for surface interactions. See specifically, Example 6, at col. 38 and also, examples 25-40 at col. 41, which discloses a cyclic peptide occurring at the R and K residues. Robinson similarly taught or at least suggests that the dimer interface can also be trp. Robinson does not disclose a zipper-like motif of the trp residues. However, Floudas discloses at paragraph [0152] that the beta sheet nucleates at the hairpin turn and proceeds to form through a zippering model that is stabilized by hydrogen bond formation. Floudas at [0153] discloses that hydrophobic interactions between beta strand residues are used to develop several optimization models that can be globally optimized to provide a rank ordered list of potential beta sheet arrangements with decreasing hydrophobic interaction energies. These formulations are classified as inter alia, a strand-based model. At paragraph [0154] it is disclosed that the strand-based formulation relies on the identification of contiguous sets of residues to define potential beta strands. These individual strands represent one component in the formation of a beta sheet configuration. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was

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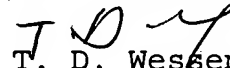
made to choose Trp-Trp as the cross-strand zipper-like motif in the method of Robinson since Robinson teaches that Trp is one of the cross-strand forming residues. As taught by Floudas this forms a zipper-like motif that are used to develop several optimization models that can be globally optimized to provide a rank ordered list of potential beta sheet arrangements with decreasing hydrophobic interaction energies. This teaching of Floudas would provide the motivation to one having ordinary skill in the art at the time of the invention.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw

November 14, 2005